pagepress

GLOBAL CARDIOLOGY
Global Cardiology 2023; **1**: 23-29
Published online 29 December 2023 | **DOI**: 10.4081/cardio.2023.14

ARTICLE

The impact of maternal congenital heart disease on pregnancy outcomes in Malta: a retrospective study

Maryanne Caruana,[1] Miriam Gatt,[2] Oscar Aquilina,[1] Charles Savona Ventura,[3] Victor Grech,[4] Jane Somerville[1]

[1]Department of Cardiology, Mater Dei Hospital, Msida; [2]Directorate for Health Information and Research, Gwardamangia; [3]Department of Obstetrics and Gynecology, University of Malta, Msida; [4]Department of Pediatrics, Mater Dei Hospital, Msida, Malta

Abstract

Background: Most female patients with congenital heart disease (CHD) are becoming pregnant. Maternal CHD can have a negative impact on mother and fetus. This is the first study investigating pregnancy outcomes in Maltese grown-up congenital heart disease (GUCH) patients and one of few to compare these with outcomes in women without heart disease.
Methods: Known GUCH pregnancies for the period of 2007-2014 were extracted from our database (GUCH cohort) and cardiovascular outcomes retrieved from hospital notes. A control cohort of 540 pregnancies in women without cardiovascular disease was generated through twenty-fold random matching based on subject age from among all pregnancies in Maltese nationals for the same 8-year period. Obstetric and offspring outcomes were compared between the two cohorts.
Results: The GUCH cohort consisted of 27 pregnancies in 24 women. Cardiovascular complications occurred in only 1/27 (3.7%) pregnancies. Elective Caesarean sections were commoner (29.6% *vs*. 15.4%) and unassisted vaginal deliveries less frequent (51.9% *vs*. 64.6%) in the GUCH cohort (p=0.02). Obstetric complication rates were similar. GUCH women had smaller babies (median 3030 g *vs*. 3230 g; p=0.045) and showed a trend towards more small-for-gestational age babies (18.5% *vs*. 8.4%; p=0.08) and congenital malformations (7.4% *vs*. 2.4%; p=0.06).
Conclusions: Despite the potential adverse effects of maternal CHD on mother and fetus, most pregnancies are uncomplicated and outcomes comparable to those in women without heart disease, particularly if baseline clinical status is good. Based on our findings, it is being proposed that prospective mothers be counselled about the possibility of having smaller infants.

Key words congenital heart defects, pregnancy, cardiovascular pregnancy complications.

Received: 8 November 2023; Accepted: 11 November 2023.
**Correspondence to: Maryanne Caruana, Cardiac Catheterisation Suite, Department of Cardiology, Mater Dei Hospital, Msida MSD 2090, Malta.*
Tel.: +35679703708 - Fax: +35625453894. E-mail: caruana.maryanne@gmail.com

Introduction

Advances in the management of congenital heart disease (CHD) have led to most patients reaching child-bearing age, with an increasing number of such women becoming pregnant.[1] The physiological changes that occur during pregnancy, including increases in blood volume, heart rate and cardiac output, represent an added cardiovascular burden which may be poorly tolerated by women with CHD, especially those with hemodynamically significant residua.[2] Such pregnancies are also at higher risk of neonatal complications.[3,4] Three main tools have been proposed for risk stratification of maternal cardiovascular complications among women with heart disease.[5] The CARPREG score and modified World Health Organization (WHO) classification can be applied to women with both CHD and acquired heart disease (AHD),[4-7] while the ZAHARA score is designed specifically for women with CHD.[8] CARPREG and ZAHARA scores consider the maternal clinical cardiac status to calculate risk of cardiovascular complications. In the modified WHO classification, pregnancies are classified into four risk groups based on specific heart lesions, with maternal risk ranging from very low in WHO class I to extremely high and warranting advice against pregnancy in class IV.[6,7]

Malta has a population of around 425,000 and the main religion is Roman Catholic.[9] Termination of pregnancy is illegal up to the time of writing of this manuscript. Malta's health care system is funded through taxation and national insurance,

© 2023 The Authors. Global Cardiology published by PAGEPress Publications.
This is an open access article under the terms of the Creative Commons Attribution-NonCommercial International License (CC BY-NC 4.0) which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

OPEN ACCESS

and specialized services, including a dedicated service for grown-ups with congenital heart disease (GUCH) are provided in one main teaching hospital. Obstetric data covering all deliveries to residents and non-residents taking place on the Maltese islands is collected and administered by the National Obstetric Information System (NOIS), which was launched by the Department of Health Information and Research in 1999.[10] There has been a trend of increasing maternal age over the past decade, with the 30-34 years' age bracket being the one with most reported deliveries (36.3%) in 2015. There were 3544 reported deliveries in women of Maltese nationality in 2015, 92.7% of all babies were born at term and the average birth weight was 3217g. Two maternal deaths were reported in the last decade.[10]

The overall incidence of CHD in Malta has been reported at around 0.8%, which is similar to that in other European countries.[11] Virtually all congenital cardiac surgery on children and adults born in Malta is carried out in overseas tertiary referral centers, in the United Kingdom, through a reciprocal National Health Service agreement. A number of structural cardiac interventions are carried out locally by visiting specialists. A GUCH service was initiated in the late 1990s and expanded considerably over the last decade. It includes a specific service for the provision of preconceptual counselling to female patients who want to get pregnant and for their management during pregnancy through close collaboration with obstetricians and anesthetists.

The aims of this retrospective study were i) to describe maternal outcomes among women with CHD in Malta and ii) to investigate the potential impact of maternal CHD on obstetric and offspring outcomes through comparison with reported outcomes in age-matched women with no history of cardiovascular disease in the general Maltese population.

Materials and Methods

All known pregnancies in women of Maltese nationality with CHD for the 8-year period 2007-2014 were retrieved from our institutional database (GUCH pregnancy cohort). Baseline characteristics, cardiac events and obstetric and offspring outcomes for these women were obtained retrospectively from hospital paper notes and digital investigation reports. An individual twenty-fold random matching based on subject age was performed out of all 29,349 pregnancies in Maltese women with no documented cardiovascular disease as collected by NOIS for the same study period. This generated the age-matched control cohort of 540 pregnancies referred to in the manuscript as *non-cardiovascular disease* (*CVD*) *pregnancy cohort*. NOIS pregnancy entries for women of non-Maltese nationality were excluded primarily to avoid any bias related to potentially differing epidemiological and/or genetic characteristics, as well as due to the possibility of their medical data leading up to the index pregnancy being incomplete. Maltese pregnancies with incomplete obstetric and/offspring outcome data were also excluded during the matching process.

The term *tachyarrhythmias* refers to any symptomatic sustained and non-sustained tachyarrhythmia and excludes incidental asymptomatic atrial/ventricular ectopy. Ventricular and valvular function was based on echocardiographic findings and follows international guidelines.[12] Left ventricular systolic dysfunction is defined as an ejection fraction <55% and right ventricular systolic dysfunction is defined as a tricuspid annular plane systolic excursion <16 mm and fractional area change <35%. Aortic outflow tract obstruction is referred to as moderate if peak velocity is 3.0-3.9 m/s and mean pressure drop is 25-40 mmHg and severe if peak velocity is ³4.0 m/s and mean pressure drop is >40 mmHg. Pulmonary outflow tract obstruction is defined as moderate if peak velocity is 3.0-4.0 m/s and severe if >4.0 m/s. Mitral regurgitation is defined as more than mild if proximal isovelocity surface area is >0.4 cm and vena contracta >0.3 cm. Aortic regurgitation is defined as more than mild if pressure half time is <500 ms and vena contracta is >0.3 cm. Pulmonary regurgitation is referred to as severe if pressure half-time is <100 ms and color flow Doppler origin of the regurgitant jet is from the bifurcation of the branch pulmonary arteries. Severity of tricuspid regurgitation is based mostly on visual assessment.

The outcomes compared between the subjects in the two study cohorts were based on those collected by NOIS. Obstetric outcomes studied were threatened abortion, threatened premature labor, antepartum hemorrhage, placenta praevia, placental abruption, suspected intrauterine growth retardation (IUGR), maternal infections, hypertensive diseases of pregnancy, gestational diabetes, need for hysterectomy within 24 hours of delivery, retained placenta, severe hemorrhage (defined as blood loss of 1 L in 2 hours), need for blood transfusion, dystocia and maternal death. Offspring outcomes studied were number of offspring per pregnancy, offspring gender, pregnancy duration, prematurity (pregnancy duration <37 weeks), small-for-gestational age (SGA) births (birth weight <10th centile for gestational age), birth weight, presence of congenital malformations diagnosed at birth and occurrence of stillbirths and neonatal death. Informed consent was obtained from all participants. The study protocol was approved by the University of Malta Research Ethics Committee and conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

Statistical methods

Categorical variables were analyzed using Chi-squared tests. Fisher's Exact test was applied in the case of smaller sample sizes. Shapiro-Wilk test applied to numerical variables (pregnancy duration and birth weight) showed a non-normal distribution. Subsequently, Mann-Whitney *U* test was used for comparison of these variables between the two study cohorts. Analyses were performed using SPSS 21 (IBM® SPSS® 21, SPSS Inc., Chicago IL, USA). All statistical analyses were two-sided and statistical significance was defined as p≤0.05.

Results

The GUCH pregnancy cohort consisted of 27 pregnancies in 24 women, with 9 pregnancies belonging to modified WHO class I, 15 pregnancies to modified WHO class II/II-III and 3 pregnancies to modified WHO class III (Table 1). Maternal baseline characteristics are summarized in Table 2. Repaired tetralogy of Fallot was the commonest congenital heart lesion, featuring in 6/27 (22.2%) GUCH pregnancies. Mean maternal age was 27.44±5.24 years (range 15-41 years). All women were in New York Heart Association (NYHA) class I prior to the index pregnancy and none had cyanosis at baseline. Three patients were on cardiac medications prior to pregnancy: two women were on aspirin and one patient was on warfarin. Only one patient – a case of atriopulmonary (AP) Fontan surgery for tricuspid atresia – had a history of prior arrhythmias in the form

Table 1. Congenital heart lesions in the 27 grown-up congenital heart disease pregnancies divided by the modified World Health Organization classification of maternal cardiovascular risk.6,7

Modified WHO class I (n=9)		Modified WHO class II/II-III (n=15)		Modified WHO class III (n=3)	
Lesion	N. (%)	Lesion	N. (%)	Lesion	N. (%)
Repaired ASD	3 (11.1)	Repaired CoA	4 (14.8)	Fontan-type palliation	2 (7.4)
Repaired PS	1 (3.7)	Repaired TOF	6 (22.2)	TGA-Mustard	1 (3.7)
Repaired pAVSD	1 (3.7)	Congenital AS	1 (3.7)		
Repaired PDA	3 (11.1)	Unoperated VSD	1 (3.7)		
Repaired TAPVD	1 (3.7)	SAS	3 (11.1)		

ASD, atrial septal defect; VSD, ventricular septal defect; PDA, patent ductus arteriosus; CoA, coarctation of the aorta; TOF, tetralogy of Fallot; PS, pulmonary stenosis; TAPVD, total anomalous pulmonary venous drainage; SAS, subaortic stenosis; TGA, transposition of great arteries; AS, aortic stenosis; pAVSD, partial atrioventricular septal defect; WHO, World Health Organization.

Table 2. Maternal baseline cardiac characteristics for the 27 pregnancies in the grown-up congenital heart disease cohort.

Maternal baseline cardiac characteristics	N. (%)
Clinical characteristics (n=27)	
Cyanosis	0 (0)
NYHA functional class I	27 (100)
History of arrhythmias	
Atrial	1 (3.7)
Ventricular	0 (0)
Permanent pacemaker/ICD *in situ*	0 (0)
History of congestive heart failure	0 (0)
Cardiac medications (n=27)	
Antiplatelets	2 (7.4)
Oral anticoagulant	1 (3.7)
Antiarrhythmics	0 (0)
Antihypertensive agent	0 (0)
Diuretics	0 (0)
Echocardiographic parameters (n=23)*	
Systemic ventricular dysfunction	0 (0)
Subpulmonary ventricular dysfunction	0 (0)
More than mild aortic outflow tract obstruction	
Moderate	1 (4.3)
Severe	0 (0)
More than mild pulmonary outflow tract obstruction	
Moderate	1 (4.3)
Severe	0 (0)
More than mild mitral regurgitation	0 (0)
More than mild aortic regurgitation	0 (0)
More than mild tricuspid regurgitation	0 (0)
More than mild pulmonary regurgitation	3 (13)

ICD, implantable cardioverter-defibrillator; NYHA, New York Heart Association.
*Complete echocardiographic data was available for 23/27 pregnancies.

of sustained atrial flutter needing direct current cardioversion in the past. Complete echocardiographic data was available for 23/27 GUCH pregnancies. In all these cases, there was good systemic ventricular function at baseline. One patient had moderate congenital aortic stenosis (AS) and another patient had moderate right ventricular outflow tract obstruction at branch pulmonary artery level, but no patients had severe outflow tract obstruction.

Cardiac events and cardiac medication use in pregnancy in the GUCH cohort is summarized in Table 3. Cardiac events were uncommon with only one patient, with a history of tricuspid atresia and AP Fontan surgery, developing paroxysmal atrial arrhythmias and heart failure. The same patient was also the only one to require antiarrhythmic therapy, low-dose diuretics and anticoagulation during pregnancy. Two other women, one with total cavopulmonary connection and one with recent percutaneous closure of an atrial septal defect remained on low-dose aspirin during pregnancy.

Tables 4 and 5 summarize the results of comparison of obstetric and offspring outcomes respectively. There were no significant differences in the frequency of pregnancy and delivery-related complications between the two cohorts. Unassisted vaginal delivery was the commonest mode of delivery in both cohorts; however, it was less common among subjects in the GUCH cohort (GUCH 51.9% *vs*. non-CVD 64.6%). Conversely, elective pre-labor Caesarean section was employed more frequently among women in the GUCH cohort (8/27; 29.6%) when compared to those in the non-CVD cohort (83/540; 15.4%). Four of the 8 Caesarean sections (50%) in the GUCH pregnancy cohort were performed for cardiac indications, 3/8 (37.5%) had obstetric indications and one was performed based on patient preference. Instrumental delivery was used for 2/27 (5.4%) GUCH pregnancies and for 20/540 (3.7%) non-CVD pregnancies. The differences in delivery methods between the two cohorts were statistically significant (p=0.02). There were more premature births in the GUCH cohort (11.1% *vs*. 4.1%) though this difference did not reach statistical significance (p=0.11). Overall pregnancy duration in the two cohorts was not significantly different (median duration GUCH 38 weeks *vs*. non-CVD 39 weeks; p=0.14). Women in the GUCH cohort gave birth to significantly smaller babies (median birth weight: GUCH 3030 g *vs*. non-CVD 3230 g; p=0.045) and showed a trend towards having more SGA babies (GUCH 18.5% *vs*. non-CVD 8.4%; p=0.08). There was also a trend towards more frequent congenital malformations among offspring born to GUCH women (7.4% *vs*. 2.4%; p=0.06).

Table 3. Cardiac events and need for cardiac medication use during pregnancy in the 27-patient grown-up congenital heart disease pregnancy cohort.

Cardiac events and medication	N. pregnancies (%)
Cardiac events	
Heart failure	1 (3.7)*
Arrhythmias requiring treatment	
Atrial	1 (3.7)*
Ventricular	0 (0)
Thromboembolic events	0 (0)
Infective endocarditis	0 (0)
Need for urgent percutaneous/surgical intervention	0 (0)
Cardiac medications used during pregnancy	
Antiplatelets	2 (7.4)
Low-molecular weight heparin	1 (3.7)*
Antiarrhythmic agent/s	1 (3.7)*
Diuretic	1 (3.7)*
Antihypertensive agent	0 (0)

*The only patient to develop significant cardiac events during pregnancy and to require anticoagulation, antiarrhythmic therapy and a diuretic was a patient with atriopulmonary Fontan for tricuspid atresia.

Table 4. Comparison of obstetric complications between grown-up congenital heart disease and non-cardiovascular disease cohorts.

Complication	GUCH pregnancies (%)	Non-CVD pregnancies (%)	p
Threatened abortion	1/27 (3.7)	28/540 (5.2)	1.00
Threatened premature labor	0/27 (0)	13/539 (2.4)	1.00
Antepartum hemorrhage	0/27 (0.0)	9/540 (1.7)	1.00
Placenta praevia	0/27 (0.0)	2/539 (0.4)	1.00
Placental abruption	0/27 (0.0)	3/540 (0.6)	1.00
Suspected IUGR	2/27 (7.4)	28/539 (5.2)	0.65
Infections	0/27 (0)	32/540 (5.9)	0.39
Gestational hypertension	0/27 (0.0)	37/540 (6.9)	0.24
Pre-eclampsia/eclampsia	0/27 (0.0)	3/540 (0.6)	1.00
Gestational diabetes	0/27 (0)	25/539 (4.6)	0.62
Hysterectomy within 24hrs	0/27 (0)	0/540 (0)	/
Retained placenta	0/27 (0)	3/540 (0.6)	1.00
Hemorrhage (1l in 2hrs)	0/27 (0)	0/540 (0)	/
Blood transfusion	0/27 (0)	2/539 (0.4)	1.00
Dystocia	0/27 (0)	1/540 (0.2)	1.00
Maternal death	0/27 (0)	0/540 (0)	/

GUCH, grown-up congenital heart disease; IUGR, intrauterine growth retardation; CVD, cardiovascular disease.

Table 5. Comparison of offspring outcomes between pregnancies in the two study cohorts.

Outcome	GUCH pregnancies	Non-CVD pregnancies	p
Singleton pregnancy	26/27 (96.3%)	527/540 (97.6%)	0.50
Male infant gender	14/27 (51.9%)	292/540 (54.1%)	0.82
Pregnancy duration, weeks*	38 (range 36-41)	39 (range 22-41)	0.14
Premature birth#	3/27 (11.1%)	22/537 (4.1%)	0.11
Small for gestational age#	5/27 (18.5%)	45/537 (8.4%)	0.08
Birth weight, g°	3027 (2821, 3232) [3030]	3212 (3168, 3256) [3230]	*0.045*
Congenital malformations	2/27 (7.4%)	13/540 (2.4%)	0.06
Still births/neonatal deaths	0/27 (0%)	5/540 (1%)	1.00

GUCH, grown-up congenital heart disease; IUGR, intrauterine growth retardation; CVD, cardiovascular disease.
*Pregnancy duration is expressed as median followed by range in weeks. #Rates of premature birth and small for gestational age babies (<10th centile for gestational age) are expressed as percentages out of all live births. °Birth weight is expressed as mean with 95% confidence intervals followed by median in square brackets.
Statistically significant differences are shown in *italics*.

Discussion

Maternal CHD is traditionally associated with poorer pregnancy outcomes, mainly through increased risk of cardiac events in the mother and complications in the fetus.[6] Neonatal complication rates of 20-28% and neonatal mortality of 1-4% have been reported among women with all forms of heart disease.[3,4,8,13,14] The commonest reported complications are premature births, small-for-gestational-age birthweights and respiratory distress syndrome. The maternal predictors of neonatal events are baseline NYHA class >II or cyanosis, maternal left heart obstruction, smoking during pregnancy, multiple gestation, use of oral anticoagulation during pregnancy and the presence of a mechanical valve prosthesis.[6] Hypertensive diseases of pregnancy and postpartum hemorrhage (PPH) are the commonest obstetric complications reported in women with heart disease.[3,13] Contrary to maternal and neonatal complications, the reported experience with obstetric complications is more variable. Whereas the CARPREG investigators found coarctation of the aorta as an independent predictor for pregnancy-induced hypertension and use of anticoagulants in the peripartum period and cyanosis as independent predictors for PPH,[4] the ZAHARA investigators found no such associations in their cohort.[8]

Adverse maternal cardiac events were only observed in one of the 27 GUCH pregnancies (3.7%) in our cohort, with the same patient developing symptomatic paroxysmal atrial arrhythmia as well as heart failure. This pregnancy was the one with the highest predicted risk in our cohort (CARPREG risk 27%; ZAHARA risk 70%; modified WHO class III). Arrhythmias and heart failure have been consistently reported as the commonest maternal cardiovascular complications.[3,4,8,15] Our cardiac event rate of 3.7% is lower than what has been reported in most large studies concentrating on pregnancy in women with CHD, where cardiac event rates ranged from 4% to 25%.[1,3,5,8,13,16,17] Although this finding is reassuring, it should be interpreted with caution as it is likely to be, at least partly, due to fewer women with more complex forms of CHD and poorer baseline cardiac status in the Maltese GUCH cohort when compared to other studies referred to earlier. In fact, both CARPREG and ZAHARA risk scores for the 23/27 patients in the Maltese GUCH cohort with complete pre-pregnancy data were low, with an overall CARPREG mean risk of 6.91±6.34% (median 5%) and an overall ZAHARA mean risk of 8.25±13.89% (median 2.9%). Similarly, only three pregnancies occurred in women considered to be at high risk of maternal cardiac complications by modified WHO classification, with all other pregnancies being in lower risk categories (Table 1).

The commonest primary cardiac lesion in our series was tetralogy of Fallot (TOF) (6/27 in 6 patients; 22.2% pregnancies), followed by coarctation of the aorta (4/27 in 3 patients; 14.8% pregnancies). No maternal cardiac events were reported in either of these groups. Right ventricular (RV) dysfunction and/or moderate to severe pulmonary regurgitation (PR) have been reported as the main risk factors for cardiac complications in pregnancies in women with TOF.[6,18-20] All our TOF patients had undergone complete repair in infancy or early childhood. Although two women had moderate PR and one had severe PR, all 6 patients were asymptomatic, and all had normal RV function at baseline. All three coarctation patients in our cohort had undergone surgical repair, and none had significant residua or hypertension prior to pregnancy. Consequently, they were all at low risk of aortic rupture and cerebral aneurysm rupture, which are the maternal complications mostly reported in this patient group.[6]

Three women went through a high-risk pregnancy: one patient with atrial switch (mustard repair) for transposition of the great arteries and two patients with Fontan-type palliation. Our only atrial switch patient had good systemic RV function, no significant TR and no previous arrhythmias, putting her in a more advantageous position for a good maternal outcome.[6,21-23] Both women with Fontan palliation had good NYHA status, retained ventricular function and no significant atrioventricular valve regurgitation at baseline, all factors considered favorable with this type of circulation.[6] However, a previous history of atrial arrhythmias requiring treatment and a possibly less efficient type of Fontan circuit (classical Fontan with right atrium to pulmonary artery conduit) in the patient

with AP Fontan resulted in a difference in occurrence of cardiac events between the pregnancies.[24] Thus, even when assessed by cardiac lesion, most of our patients tolerated pregnancy without maternal complications, largely because their anatomy and function at baseline put them at the more favorable end of the spectrum.

Our study is one of few in the literature to compare pregnancy outcomes in GUCH patients with those in contemporary women without heart disease from the same population.[1,14,17,25] There were significantly more deliveries by Caesarean section and fewer normal vaginal deliveries in our GUCH cohort, which compares to the reported literature.[1,14,17,25] There was no excess of obstetric complications in our GUCH pregnancy cohort when compared to non-CVD women (Table 4). These findings are similar to those reported in the Canadian study by Siu *et al.,*[14] the German study by Hrycyk *et al.*[25] and those stemming from the Registry of Pregnancy and Cardiac Disease (ROPAC).[17] Conversely, in their nationwide U.S. study from 2015, Thompson *et al* found the odds of several obstetric complications, including gestational diabetes, preterm labor, placental abruption and postpartum hemorrhage, to be significantly higher among delivery hospitalizations for women with CHD.[1]

Overall, neonatal outcomes in our GUCH cohort were good and, in the main, not significantly worse than those in the non-CVD cohort. Although there was a higher rate of premature births in our GUCH cohort (11.1% *vs*. 4.1%), this difference did not reach statistical significance (p=0.11). Furthermore, the lowest pregnancy duration observed was only 36 weeks and there were no cases of severe prematurity. This contrasts with the observations made by other studies where higher rates of premature births in GUCH pregnancies,[4,26] as well as significantly more premature births when compared to women without heart disease, were reported.[14,17] However, it should be noted that some of these studies included other forms of heart disease apart from CHD and had a higher proportion of women with a less favorable baseline maternal status and thus a higher propensity for poorer neonatal outcomes.

The main difference in offspring outcomes observed between patient and control cohorts related to significantly smaller babies born to women with CHD (median birth weight GUCH 3030 g *vs*. non-CVD 3230 g; p=0.045). There was also a trend towards more babies being small-for-gestational age in the GUCH cohort (18.5% *vs*. 8.4%; p=0.08). This observation has been documented by several other studies.[17,25,27] Maternal cyanosis and poor cardiac output are recognized as the main risk factors for fetal growth restriction and lower birth weights.[27] The fact that, on the whole, our GUCH cohort consisted of women with good saturations and satisfactory cardiac output at baseline, and that use of medications linked with IUGR was minimal, suggests that there might be other less well-recognized factors coming into play to interfere with fetal growth in mothers with CHD. It could also be argued that the *cardiologist's definition* of good cardiac output based on imaging and functional status might not necessarily translate into equally good uteroplacental flow.

Limitations

The small Maltese GUCH population and the even smaller numbers of female patients that became pregnant during the study period, which in themselves are an inevitable consequence of the small size of the country, represent the main limitation of this study. It is possible that some women with CHD of mild complexity who were not under regular specialist follow-up and were deemed to be at very low risk in pregnancy might have delivered in private centers and thus failed to be included due to lack of documentation in hospital records. Notwithstanding, the fact that most Maltese deliveries on the islands take place in state-run hospitals irrespective of maternal or obstetric risk makes it likely that missed GUCH pregnancies were few and that only women with mild or trivial lesions were selected out. A further limitation is the retrospective nature of the study which resulted in some patients having incomplete data, though this was limited to few patients who were not under regular specialist clinical follow-up. The comparison of outcomes between GUCH and non-CVD cohorts relied on outcomes routinely collected by NOIS. Because NOIS only captures pregnancies that end in the birth of a baby of ≥22 completed weeks, comparison of miscarriage rates could not be performed.

Conclusions

Although pregnancy in the presence of maternal CHD can be of higher risk to mother and fetus, our findings reinforce the fact that, with careful preconceptual counselling and close monitoring by a specialist team of cardiologists, obstetricians and anesthetists, pregnancy outcomes can be comparable to those in women without heart disease. The presence of maternal CHD appears to predispose to lower infant birth weight, even in women with less complex disease and good baseline functional status. While risk-predicting tools are a helpful guide, advice to prospective mothers needs to be tailored to the individual patient's case, taking into account not only the woman's functional status but also the services and infrastructure of the institution where the pregnancy will be followed and delivery performed so as to ensure safety at all stages.[28] Finally, large multi-center collaborations like the European Society of Cardiology's ROPAC which also include data about follow-up after pregnancy,[29] will help shed more light on the long-term impact that pregnancy could have on cardiac function in women with CHD, particularly in an era where access to assisted reproductive technology, often with use of hormonal therapy and a higher possibility of multiple pregnancies, is increasing in many countries.

Contributions

The authors contributed equally.

Conflict of interest

The authors declare no potential conflict of interest.

References

1. Thompson JL, Kuklina EV, Bateman BT, Callaghan WM, James AH, Grotegut CA. Medical and Obstetric outcomes among pregnant women with congenital heart disease. Obstet Gynecol 2015;126: 346-54.
2. Moghbeli N, Pare E, Webb G. Practical assessment of maternal cardiovascular risk in pregnancy. Congenit Heart Dis 2008;3:308-16.
3. Khairy P, Ouyang DW, Fernandes SM, Lee-Parritz A, Economy KE, Landzberg MJ. Pregnancy outcomes in women with congenital heart disease. Circulation 2006;113:517-24.
4. Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation 2001;104:515-21.
5. Lu CW, Shih JC, Chen SY, et al. Comparison of 3 risk estimation methods for predicting cardiac outcomes in pregnant women with congenital heart disease. Circ J 2015;79:1609-17.
6. Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, et al. ESC guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J 2011;3:3147-97.
7. Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart 2006;92:1520-5.
8. Drenthen W, Boersma E, Balci A, Moons P, et al. Predictors of pregnancy complications in women with congenital heart disease. Eur Heart J 2010;31:2124-32.
9. National Statistics Office. Malta in figures 2014. Available from: http://nso.gov.mt/en/publicatons/Pages/Publications-by-Date.aspx. Accessed on:
10. Directorate for Health Information and Research. National obstetrics information system 2016. Available from: https://healthservicescms.gov.mt/en/dhir/Documents/1st%20Quarter%20Report%20-%202016.pdf
11. Grech V. Spectrum of congenital heart disease in Malta. An excess of lesions causing right ventricular outflow tract obstruction in a population-base study. Eur Heart J 1998;19:521-5.
12. British Society of Echocardiography. Protocols and guidelines 2016. Available from: https://www.bsecho.org/education/. Accessed on:
13. Drenthen W, Pieper PG, Roos-Hesselink JW, et al. Outcome of pregnancy in women with congenital heart disease: a literature review. J Am Coll Cardiol 2007;49:2303-11.
14. Siu SC, Colman JM, Sorensen S, et al. Adverse neonatal and cardiac outcomes are more common in pregnant women with cardiac disease. Circulation 2002;105:2179-84.
15. Avila WS, Rossi EG, Ramires JA, et al. Pregnancy in patients with heart disease: experience with 1,000 cases. Clin Cardiol 2003; 26:135-42.
16. Opotowsky AR, Siddiqi OK, D'Souza B, Webb GD, Fernandes SM, Landzberg MJ. Maternal cardiovascular events during childbirth among women with congenital heart disease. Heart 2012;98: 145-51.
17. Roos-Hesselink JW, Ruys TP, Stein JI, et al. Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European Society of Cardiology. Eur Heart J 2013;34:657-65.
18. Balci A, Drenthen W, Mulder BJ, et al. Pregnancy in women with corrected tetralogy of Fallot: occurrence and predictors of adverse events. Am Heart J 2011;161:307-13.
19. Veldtman GR, Connolly HM, Grogan M, Ammash NM, Warnes CA. Outcomes of pregnancy in women with tetralogy of Fallot. J Am Coll Cardiol 2004;44:174-80.
20. Pedersen LM, Pedersen TA, Ravn HB, Hjortdal VE. Outcomes of pregnancy in women with tetralogy of Fallot. Cardiol Young 2008;18:423-9.
21. Drenthen W, Pieper PG, Ploeg M, et al. Risk of complications during pregnancy after Senning or Mustard (atrial) repair of complete transposition of the great arteries. Eur Heart J 2005;26:2588-95.
22. Canobbio MM, Morris CD, Graham TP, Landzberg MJ. Pregnancy outcomes after atrial repair for transposition of the great arteries. Am J Cardiol 2006;98:668-72.
23. Trigas V, Nagdyman N, Pildner von Steinburg S, et al. Pregnancy-related obstetric and cardiologic problems in women after atrial switch operation for transposition of the great arteries. Circ J 2014;78:443-9.
24. Caruana M, Grech V, Somerville J. Pregnancy in atriopulmonary connection and total cavopulmonary connection - a comparison of two cases. Cardiol Young 2012;22:600-2.
25. Hrycyk J, Kaemmerer H, Nagdyman N, Hamann M, Schneider K, Kuschel B. Mode of delivery and pregnancy outcome in women with congenital heart disease. PloS One 2016;11:e0167820.
26. Stangl V, Schad J, Gossing G, Borges A, Baumann G, Stangl K. Maternal heart disease and pregnancy outcome: a single-centre experience. Eur J Heart Fail 2008;10:855-60.
27. Gelson E, Curry R, Gatzoulis MA, et al. Effect of maternal heart disease on fetal growth. Obstet Gynecol 2011;117:886-91.
28. Greutmann M, Pieper PG. Pregnancy in women with congenital heart disease. Eur Heart J 2015;36:2491-9.
29. Greutmann M, Silversides CK. The ROPAC registry: a multicentre collaboration on pregnancy outcomes in women with heart disease. Eur Heart J 2013;34:634-5.

This manuscript was originally published in the *International Cardiovascular Forum Journal*, which has now ceased publication.
It has been given permission to be published in *Global Cardiology* in a revised form.